REMARKS

Claims 1, 4, 7, 8, 11-14, 20, 21, 23-27, 29-32, 37-41 and 51-59 are in the application. Claims 1, 4, 7, 8, 11, 12, 13, 20, 21, 23, 24, 26, 27, 29, 30, 31 have been amended. Claims 3, 5, 6, 9, 10, 15-19, 22, 28 and 33-36 have been cancelled. Claims 52 to 59 have been added. Support for the amendments lies in the claims as originally filed, or in the working examples. No new matter is believed added. Applicants reserve their right to file divisional or continuation applications on all cancelled or deleted subject matter.

Rejection under 35 USC §112

Claims 11, 12, 29 and 30 are rejected under 35 USC §112 as being indefinite. Claims 11 and 29 contain the trademark Cab-O-Sil and Syloid. Cab-O-Sil is a synonym for colloidal silicon dioxide, and Syloid is a brand name for silica gel. Copies of the Pharmaceutical Handbook of Excipients and the web page for W.R. Grace accompany this response for substantiation. The claims have been amended accordingly.

Reconsideration and withdrawal of the rejection to the claims under 35 USC §112 is respectfully requested in view of the amendments herein.

Rejection under 35 USC §103

Claims 1, 3-7, 9-25 and 27-41 are rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190). Applicants respectfully traverse this rejection.

Claims 8 and 26 are re rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and De Bock et al. (US 5, 428, 150). Applicants also respectfully traverse this rejection.

The Breitenbach et al. patent is directed to a tablet which comprises as the foaming polymer a thermoplastic polymer selected from a water-soluble, melt processable homo or copolymer of N-vinylpyrrolidone or mixtures of such polymers (see Column 2, lines 58-60). While the polymers can contain other co-monomers, those co-

monomers are vinyl acetate, or acrylic acid (see column 2, lines 64-66 and column 3, lines 1 to 15).

While the preparation can contain other excipients, such as plasticizers (column 3, lines 43-49), bulking agents (Column 3, lines 33-37), and lubricants (column 3, lines 53-55), etc. the primary polymer remains N-vinylpyrrolidone.

Applicants have amended Claim 1 to require the specific polyol and non-thermosetting modifier and/or non-thermosetting polymer to better clarify and claim the invention. The equivalent dependent claims have been cancelled.

Breitenbach et al. requires a thermoplastic polymer which is N-vinylpyrrolidone. The present invention does not use such as polymer. The present invention is the novel combination of agents which when prepared in a manner as described in the specification produce a microcellular foamed tablet containing an active pharmaceutical agent.

A significant difference between the present invention and Breitenbach et al. is that microcellular foam tablets of the present invention are formed in-situ, by first intent, in a novel injection molding process (as described herein). Breitenbach et al. prepares thermoplastic foam extrudates in a conventional extruder. The extrudates are then shaped into forms by secondary processes, i.e., cutting, chopping, punching (see column 5, lines 31 to 61). Consequently, the formulation and the process of using this formulation to make injection molded tablets is fundamentally different.

As noted, Breintenbach et al. uses foaming agents to prepare expanded extrudates that Breintenbach et al. then utilizes a secondary process to turn into a pharmaceutical form. In column 5 lines 2 to 5: "The foamed active ingredient preparation is subsequently shaped to the required active ingredient forms in each case, for example by pelleting, granulating or tableting by known processes." In contrast, the present invention forms a foamed "active ingredient form" in-situ in the mold cavity by injection molding, in single process. Breintenbach et al. represents formulations that use an extrusion process NOT an injection molding process to make the final pharmaceutical forms, and therefore as these processes are two fundamentally different the formulations for use in those processes are also fundamentally different.

In the present invention the active pharmaceutical agent, the polyol and the non-thermosetting polymer and/or modifier take the form of a rigid microcellular foam. In

one aspect of this invention the resulting tablet can be a composition which will dissolve substantially immediately in the mouth upon oral administration. The microcellular foam matrix is particularly well suited for use in these flash-dissolving type tablets. Its cellular structure promotes quick solution, but it is much less friable than the materials used in conventional flash-dissolve tablets and those more commercially useable.

The Breintenbach et al. polymers are classic polymeric thermoplastic materials (PVP and it derivatives). Taking a definition from Plastic Injection Molding, Material Selection and Product Design Fundamentals, Douglas Bryce, Society of Manufacturing Engineers, 1997:

> THERMOPLASTIC is defined as "A plastic material which. when heated, undergoes a PHYSICAL change. (emphasis added) It can be reheated, and reformed, over and over again."
> In contrast THERMOSET (another way of saying NON-THERMOPLASTIC) is defined as "A plastic material which when heated, undergoes a CHEMICAL change and "cures". (emphasis added) It cannot be reformed and reheating only degrades it."

The presently claimed invention employs the novel use of thermosetting agents, such as polyols, starches, maltodextrins that, in the process of the invention can be injection molded into foamed tablets despite the fact they are not thermoplastic. This is an unexpected and a novel invention.

The process also employs a unique forming agent (supercritical CO_2 or N_2). As compared to the Breintenbach et al. patent the supercritical fluid dissolves in the melted mass (in the high pressure environment of the injection molder screw) to form a single-phase material. The Breintenbach et al. foaming agents are added to the relatively low pressure twin-screw extruder, these are simple mixtures that cannot attain the same degree of microcellular foam structure of the present invention, which is also a unique feature herein.

In summary, Breintenbach et al. discloses an extrusion process to prepare foams that require further processing (like standard compression into tablets) to turn them into something useful. The present invention provides for foamed tablets in a mold cavity in a

single operation using equipment significantly different from an extruder. The resulting tablet is a high quality, better controlled tablet.

Consequently, the Breitenbach et al. reference does not teach the specific combination of a polyol and the non-thermoplastic polymer or modifier as the matrix of the resulting tablet.

The secondary reference, Jane et al. does not remedy the lack of teaching absent in Breitenbach. The Jane reference discloses a thermoplastic composition based upon a soy protein. The present application does not use a soy protein. Jane et al. provides for additional excipients which can include other fillers and plasticizing agents, but again still requires as the basic polymer, a soy protein.

Neither the Breitenbach nor the Jane reference alone or in combination teach the specific combination of a polyol and the non-thermoplastic polymer or modifier as the matrix of the resulting tablet.

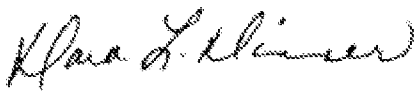
The other secondary reference, De Bock et al. (US 5, 428, 150) teaches a starch based formulation which can be extruded. There is no disclosure of this composition being used with a supercritical fluid to form a microcellular foam product. The only disclosure is to combine the composition with a thermoplastic polymeric material (column 5, lines 9-13). De Bock et al. does not teach, nor suggest, the inclusion of an active pharmaceutical agent in the resulting article. There is no teaching or suggestion to turn the compositions of DeBock et al. into a pharmaceutical dosage form. Consequently, neither Breitenbach et al. in combination with Jane et al. or De Bock et al. provides the limitations of Claim 1 herein.

In view of these remarks and amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any

additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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